Paper No. 50

# UNITED STATES PATENT AND TRADEMARK OFFICE

## BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte RICHARD M. LAWN,
GORDON A. VEHAR, and
KAREN L. WION



Appeal No. 2001-0448
Application No. 08/444,934

ON BRIEF

Before WINTERS, MILLS, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

An oral hearing in this case was scheduled for August 13, 2002. Upon reviewing the case, however, we have determined that an oral hearing will not be necessary and we render the following decision based on the record. See 37 CFR § 1.194(c).

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 4, 6, 8, 20, 21, 23, 27, 28, 31, 34-36, and 38-41. Claims 5, 24, 25, 29, 32, 33, and 37 are also pending: claims 24 and 25 have been allowed and claims 5, 29, 32, 33, and 37 have been objected to as dependent on a

rejected base claim, but the examiner has indicated that these claims would be allowable if presented in independent form.

Claim 41 is representative of the claims on appeal and reads as follows:

41. Recombinant human tissue factor protein comprising an amino acid sequence from amino acid residue one to amino acid residue 219 as provided in Figure 2, wherein the tissue factor protein has activity in a clotting assay with human plasma.

The examiner relies on the following references:

Fisher et al. (Fisher), "Cloning and Expression of Human Tissue Factor cDNA," Thrombosis Research, Vol. 48, pp. 89-99 (1987)

Scarpati et al. (Scarpati), "Human Tissue Factor: cDNA Sequence and Chromosome Localization of the Gene," Biochemistry, Vol. 26, pp. 5234-5238 (1987)

Spicer et al. (Spicer), "Isolation of cDNA clones coding for human tissue factor: Primary structure of the protein and cDNA," Proc. Natl. Acad. Sci. USA, Vol. 84, pp. 5148-5152 (1987)

Claims 4, 6, 8, 20, 21, 23, 27, 28, 31, 34-36, and 38-41 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description in the specification. We reverse.

Background

"In the extrinsic pathway of blood coagulation, tissue factor, also referred to as tissue thromboplastin, is released from damaged cells and activates factor X in the presence of factor VII and calcium." Specification, page 3. "Tissue factor is an integral membrane glycoprotein which, as discussed above, can trigger blood coagulation via the extrinsic pathway. Tissue factor consists of a protein component . . . and a phospholipid." Id.

The specification discloses cloning and sequencing of cDNA encoding human tissue factor. See Examples 1 and 2, pages 30-36. The complete DNA and amino acid sequences for the gene and protein, respectively, are disclosed. See Figure 2. The specification also discloses a hydropathy profile (Figure 5), based on which Appellants concluded that "a striking cluster of hydrophobic residues near the carboxy terminus . . ., encompassing amino acids 220-243, probably comprises the membrane anchoring domain." Pages 34-35.

Finally, the specification discloses that certain tissue factor derivatives were considered to be part of the disclosed invention, including derivatives in which the transmembrane domain was deleted. See, e.g., page 1: "This invention is also directed to tissue factor protein derivatives, particularly derivatives lacking the near C-terminal hydrophobic portion of the protein." See also

- page 7, lines 11-16: "This invention is further directed to novel tissue factor protein derivatives, in particular derivatives lacking the signal sequence and the hydrophobic portion of the protein near the C-terminal end of the protein comprising the amino acid sequence which constitutes the tissue factor protein transmembrane or membrane binding domain."

- page 12, line 31 to page 13, line 5: "Deletions are characterized by the removal of one or more amino acid residues from the tissue factor protein sequence. . . . Another deletion is of the transmembrane domain located at about residues 220 to 242 of the tissue factor protein molecule."

- page 15, lines 20-35: "A major class of substitutional or deletional variants are those involving the transmembrane, i.e. hydrophobic or lipophilic, region of tissue factor protein. . . . Deletion or substitution of the transmembrane domains [sic] will facilitate recovery and provide a soluble form of recombinant tissue factor

> protein. . . . Preferably, the transmembrane domain is deleted, rather than substituted."

Discussion

The claims on appeal are directed to human tissue factor protein and derivatives thereof, where the derivatives comprise at least the extracellular domain of tissue factor, i.e., amino acids 1-219. The examiner rejected these claims on the basis that the specification provided an inadequate written description of the claimed derivatives. See the Examiner's Answer, pages 4-5:

> [T]he specification and the original claims describe in clear and specific detail a variant of the tissue factor protein wherein amino acids 220-243, which define the transmembrane domain, are deleted. However, the specification does not describe or even suggest making a variant of tissue factor consisting of a tissue factor having from at least amino acid 1 to at least amino acid 219 or a tissue factor having an amino acid sequence from . . . amino acid 1 to between residues 220-263.

The examiner explained that the tissue factor structure described in the specification consists of three domains: an extracellular domain, an intracellular or cytoplasmic domain, and a transmembrane domain separating the other two. The examiner took the position that the specification, in referring to tissue factor derivatives formed by "deleting" the transmembrane domain, describes a derivative having the extracellular domain and the intracellular domain, coupled directly without an intervening transmembrane domain. Examiner's Answer, pages 5-6. See also page 8:

> [The relevant passages from the specification] omit reference to truncating the tissue factor protein at the hydrophobic portion and, without inclusion of any statement regarding the deletion of the hydrophilic intracellular domain, these passages specify that only the hydrophobic portion (residues 220-243) should be removed

> from the tissue factor protein. . . . The specification does not indicate that the tissue factor protein should be truncated at the transmembrane domain or that both the transmembrane domain and the intracellular domain should be deleted, resulting in the extracellular domain being by itself.

(Emphasis in original.)

Appellants argue that

> the Examiner's position is contradictory to the understanding of those skilled in the art. There was no known function for the cytoplasmic domain. The easiest way to delete the transmembrane region was to make a construct that simply stopped at amino acid 219, thereby deleting both the transmembrane domain and the cytoplasmic domain, or any portion thereof. The examiner's interpretation that one would add back in the DNA sequence encoding the cytoplasmic domain, not known to serve any function, therefore makes no sense.

Appeal Brief, page 14 (emphasis in original). In support of their position, Appellants have submitted a declaration under 37 CFR § 1.132 by William Konigsberg. Dr. Konigsberg declares that, in his opinion, "those of skill in the arts of proteins, cloning and expression, and tissue factor at that time would have understood the descriptions of deletion of the transmembrane region of tissue factor to include tissue factor proteins from which the entire C-terminal region, including the transmembrane and cytoplasmic regions, had been deleted." ¶ 5.

Dr. Konigsberg goes on to explain the basis of his conclusion, as follows:

> At the time, it was understood that transmembrane proteins generally functioned in one of two ways. In the first, the main activity of the protein resides in the extracellular domain, with the transmembrane domain serving to merely anchor the extracellular domain. In this scheme, the cytoplasmic domain is essentially irrelevant.

Id. In the other type of transmembrane proteins (e.g., receptors), the

transmembrane domain serves to conduct a signal from outside the cell to the cytoplasmic domain, which propagates the signal inside the cell. Dr. Konigsberg states that, based on the "overall structure of tissue factor as described in the specification . . . those of skill in the art at the time would have understood, that deletion of the transmembrane region is equivalent to deletion of both the transmembrane region and the cytoplasmic region, since the cytoplasmic domain serves no purpose in the absence of the transmembrane domain." Id.

The examiner "agree[d] with Dr. Konigsberg's statement of the function of transmembrane domains." Examiner's Answer, page 19. However, she did not find the declaratory evidence persuasive. The examiner noted that Dr. Konigsberg did not "state that the specification explicitly describes a tissue factor variant having amino acids 1-219 or amino acids 1 to between 219 and 263." Examiner's Answer, page 13. Rather, the declaration "only indicates that such a variant would have been considered from the description of deletion of amino acids 219-242 which make up the transmembrane domain." Id., page 19 (emphasis in original). The examiner cited several references disclosing, like the instant specification, that the tissue factor transmembrane domain is made up of amino acids 220-243, and concluded that, contrary to Dr. Konigsberg's declaration, "reference to 'deletion of the transmembrane domain' would have been understood to mean residues 220-243 and no others." Id., page 20.

It is well-settled that the written description requirement of 35 U.S.C. § 112, first paragraph, can be satisfied without express or explicit disclosure of a later-claimed invention. See, e.g., In re Herschler, 591 F.2d 693, 700, 200

USPQ 711, 717 (CCPA 1979): "The claimed subject matter need not be described in haec verba to satisfy the description requirement. It is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented processes including those limitations." (citations omitted). See also Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue.").

At the same time, it is also well-settled that a disclosure "that merely renders the later-claimed invention obvious is not sufficient to meet the written description requirement; the disclosure must describe the claimed invention with all its limitations." Tronzo v. Biomet Inc., 156 F.3d 1154, 1158, 47 USPQ2d 1829, 1832 (Fed. Cir. 1998). See also In re Winkhaus, 527 F.2d 637, 640, 188 USPQ 129, 131 (CCPA 1975) ("That a person skilled in the art might realize from reading the disclosure that such a step is possible is not a sufficient indication to that person that that step is part of appellants' invention. Such an indication is the least that is required for a description of the invention under the first paragraph of § 112." (emphasis in original)).

It is not always easy to distinguish a disclosure that adequately describes the invention, even though not in haec verba, from a disclosure that merely renders obvious a claimed invention, and therefore fails to adequately describe it. Here, the specification describes "deleting" the transmembrane domain and the

issue is whether that description shows possession of tissue factor variants deleted for both the transmembrane domain and the cytoplasmic domain.

This issue might present a difficult decision, if all we had to consider were unsupported assertions from the examiner and Appellants. Fortunately, we have more. Appellants have submitted a declaration by Dr. Konigsberg, whose background shows that he is eminently qualified to speak to the understanding of those of ordinary skill in the art. Dr. Konigsberg declared his opinion that those of skill in the art "would have understood the descriptions of deletion of the transmembrane region of tissue factor to include tissue factor proteins from which the entire C-terminal region, including the transmembrane and cytoplasmic regions, had been deleted." ¶ 5.

In addition, Dr. Konigsberg provided a rational, scientific explanation for how he reached that conclusion. He explained that the structure of the tissue factor protein, as described in the specification, would have indicated to those of skill in the art that its cytoplasmic domain was essentially irrelevant to its biological activity. See ¶ 5. Based on this understanding, he stated that those skilled in the art would have viewed the specification's description of deleting the transmembrane domain to also include deleting both the transmembrane and cytoplasmic domains.

We find Dr. Konigsberg's declaratory evidence to be credible and convincing. The examiner has provided no evidence in rebuttal, and in fact agreed with Dr. Konigsberg's statements regarding the function of transmembrane domains. In essence, the examiner seems to have agreed with

the factual statements in the declaration but disagreed as to the conclusion to be drawn from those facts. However, the examiner provided no rebuttal evidence or contrary scientific explanation as to why those of skill in the art would not interpret the facts in the same way as Dr. Konigsberg. The examiner instead seemed to rest her case on the lack of "explicit" or "inextricabl[e]" disclosure of the specific tissue factor derivative now claimed. See the Examiner's Answer, pages 12, 19. As discussed above, though, an in haec verba description is not required to satisfy the written description requirement.

Based on the record before us, we cannot say that a preponderance of the evidence supports the examiner's position. Therefore, we reverse the rejection under 35 U.S.C. § 112, first paragraph.

Other Issues

We note that the Appeal Brief discloses an interference related to the present appeal. According to PTO records, that interference (No. 103,203) was terminated September 29, 2000, with adverse judgments against the involved patent and one involved application, and a favorable judgment with respect to the second involved application. PTO records also show that the application receiving the favorable judgment is still under examination. Upon return of this application, the examiner should consider what effect, if any, that application has with respect to the claims of the instant application. The examiner should consider, for example, whether the other application would be prior art under 35 U.S.C. § 102(e) with respect to the instant claims, whether the two sets of claims

are potentially interfering, and whether the two applications present any double patenting issues.

Summary

The evidence of record shows that those of skill in the art would have understood the specification's description of deleting the transmembrane domain of tissue factor to include deleting both the transmembrane domain and the cytoplasmic domain. Therefore, the rejection for inadequate written description is reversed.

REVERSED

SHERMAN D. WINTERS )
Administrative Patent Judge )
)
)
DEMETRA J. MILLS ) BOARD OF PATENT
Administrative Patent Judge ) APPEALS AND
)
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